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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,111	SCHENDEL ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-30 and 32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-30 and 32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/18/09 3/20/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 23, 24. 27, -29, 33, 35, 38, 40-42 have been amended. Claims 23-30 and 32-46 are pending and under consideration.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 26, 27, 28, 30, 32-35, 37-40, 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen (WO98/33527, reference of the IDS filed April 29, 2004, cited in a previous Office action).

Cohen teaches a method of treating a tumor in a mammal comprising the administration of an immunogen comprising semi-allogeneic immunogenic cells (abstract and page 10, lines 1-5) Cohen teaches that the immunogenic cells of the invention encompass an antigen-presenting cell, such as a dendritic cell , which may be transformed with DNA encoding at least one antigen recognized by T-cells of the recipient (page 17, lines 1-6, page 18, lines 7-10 and page 18, lines 16-21).

Cohen teaches that the introduction of DNA into antigen-presenting cells can be accomplished through various well known procedures such as by transfection of viral and

retroviral vectors comprising the DNA, transduction into a cell of modified virus particles, and physical/chemical techniques such as calcium phosphate transfection, complex formation with polycations or lipids, electroporation, particle bombardment and microinjection into nuclei (page 29, first paragraph) and the incorporation of DNA or RNA encoding for at least one tumor antigen introduced into an antigen presenting cell (page 30, lines 1-3 and 7-8) as well as the transduction of tumor genomic DNA obtained from a tumor cell line or a tumor taken from a recipient into the antigen presenting cell (page 8, lines 8-11 and page 30, lines 11-16) which fulfills the specific embodiment of introduction of DNA encoding proteins or peptide which are over expressed in tumor cells or are derived from autologous tumor cells into the haploidentical antigen presenting cells

Cohen teaches that the neoplasm which can be treated by the inventive method include breast cancer, prostate cancer, colon cancer, esophageal cancer, ovarian cancer, melanomas, lymphomas, leukemias etc. (page 8, lines 14-24) which fulfills the specific embodiments of claims 28 34, 43 and 44. Cohen teaches that a preferred dose of semi-allogeneic APC is at least about 1 X 10^3 to about 5 X 10^9 cell per dose (page 37, lines 4-8). Cohen teaches that a tumor-inhibiting amount of the semi-allogeneic cells of the invention can be administered to patients by intravenous or subcutaneous routes (page 36, line 28 to page 37, line 17) which meets the specific embodiments of claim 37.

Cohen teaches that coding sequences for specific tumor antigens expressed in the tumor to be treated can be introduced into the semi-allogeneic APC of the invention, and that said coding sequences include the genes for Muc-1 and Her-2 (page 27, line 26 to page 28, line 14)

Cohen teaches that the semi-allogeneic determinant of the APC comprise a MHC determinant that is syngeneic to the recipient and a MHC determinant that is allogeneic to the recipient (page 19, lines 22-29). Cohen teaches that a syngeneic MHC allele coding for an HLA specificity that matches and is immunologically compatible with at least one of a MHC allele of a recipient and allogeneic refers to an HLA allele coding to an HLA-specificity that is unmatched or immunologically incompatible with the MHC allele of the recipient (page 19, line 29 to page 20, line 6). Cohen teaches that the human MHC locus is found on chromosome 6 and contains closely linked genes(page 20, first full paragraph). Cohen teaches that there is a great degree of polymorphism with each gene, and therefore a normal human population will have a

large number of genotypes (page 20, lines 17-22). Cohen teaches that a "haplotype" is a set of linked MHC genes on one chromosome 6 and because an individual inherits one maternal and on paternal chromosome 6, one haplotype is derived from each parent (page 20, lines 22-26). Cohen teaches that a preferred embodiment of donor specificities is unmatched in the range of about 50% to less than 100% (page 23, first full paragraph) a. Cohen does not specifically teach the use of haploidentical antigen-presenting cells for transfection with tumor-derived DNA.

It would have been prima facie obvious at the time that the invention was made to select a maternal or paternal antigen presenting cell which is haploidentical to the patient for transfection with tumor-derived DNA and administration to said patient. One of skill in the art would have been motivated to do so because Cohen teaches that the paternal or maternal APC would be haploidentical with the patient and therefore be semi-allogeneic, and also fulfill the specific embodiment of Cohen requiring donor specificities being unmatched in the range of 50%, because the haploidentical APC would be unmatched in the range of 50%. One of skill in the art would have been motivated to do so in order to quickly provide a donor APC which was semi-allogeneic rather than having to recombinantly construct such a donor cell, or search for a semi-allogeneic cell unrelated donor. It would have been further obvious to use antigen-presenting cells from both parent for the method of treating the patient in order to have enough semi-allogeneic APC to provide a therapeutic dose, thus fulfilling the specific limitations of claims 26 and 35.

Claims 23, 25-28, 30, 32-40, 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen (WO98/33527) as applied to claims 23, 26-28, 30, 32-35, 37-40, 43-46 above, and in further view of Eastman et al (WO 01/36680, cited in a prior action) and Schuller et al (WO 02/36790, cited in a prior action).

Claims 25 and 36 embody the method of claim 23 and the method of claim 35, respectively, wherein the first RNA from tumor cells cDNA, the cDNA is amplified by RCR and transcribed into RNA.

Cohen teaches the introduction of DNA into antigen presenting cells by viral transfection of vector comprising DNA. Cohen does not specifically teach the reverse transcription of amplified cDNA into RNA.

Eastman et al teach a method for preparing cRNA comprising amplification of cDNA (claim 3). Schuller et al teach a method of infected dendritic cells with influenza virus vector wherein said vector incorporates RNA (claims 1, 11 and 12 and page 19, lines 28-30).

It would have been prima facie obvious to substitute the influenza viral vector of Schuller et al comprising RNA obtained by reverse transcribing cDNA as taught by Eastman et al in the method Cohen.. One of skill in the art would have been motivated to dos o by the teachings of Schuller et al on the transfection of dendritic cells with the influenza virus vector which incorporates RNA and the teachings of Eastman et al on the method of making cRNA, which would provide the RNA for incorporation into said vector.

Claims 23, 24, 26-30, 32, 33-35, 37-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen (WO98/33527) as applied to claims 23, 26-28, 30, 32-35, 37-40, 43-46 above, and in further view of Warnier et al (WO 98/58956, cited in a prior action).

Claim 24 embodies the method of claim 23 wherein proteins, peptides, RNA, DNA or cDNA from several different tumor cell lines are introduced into the haploidentical antigen-resenting cells. Claim 29 embodies the cell of claim 27 wherein said cell comprises p proteins, peptides, RNA, DNA or cDNA from several different tumor cell lines. Claim 41 embodies the method of claim 23 wherein proteins, peptides, RNA, DNA or cDNA from several different tumor cell lines are introduced into the haploidentical antigen-resenting cells. Claim 42 embodies the method of claim 41 wherein pooled cRNA from two or three different tumor cell lines is introduced.

Cohen et al teach the incorporation of DNA or RNA encoding for at least one tumor antigen introduced into an antigen presenting cell (page 30, lines 1-3 and 7-8) as well as the transduction of tumor genomic DNA obtained from a tumor cell line or a tumor taken from a recipient into the antigen presenting cell (page 8, lines 8-11 and page 30, lines 11-16). Cohen does not specifically teach using polynucleotides or polypeptides from several different tumor cell lines, although Cohen et al does teach using at least one tumor antigen which is suggestive of using multiple tumor antigens.

Warnier et al teach that tumors express a set of tumor antigens, of which only certain subsets may be expressed in the tumor of any given patient and the desirability of having

antigen-presenting cells expressing "polytopes" comprising multiple epitopes on tumor antigens in order to reflect a boarder spectrum of tumor associated antigens (page 20, line 31 to page 21, line 7)

It would have been prima facie obvious at the time the clamed invention was made to use haploidentical antigen presenting cells comprising polynucleotides from more than one tumor cell line. One of skill in the art would have been motivated to do so by the teachings of Warnier et al on the restricted expression of antigen on patient tumors. One of skill in the art would have been motivated to include the antigens from several different tumor cell lines in order to insure that the antigen–presenting cell would provide antigens which were expressed on the actual patient tumor.

The rejection of claims 23, 24, 27, 28, 29, 30, 32-35, 37, 40, 41, 43 and 44 under 35 U.S.C. 102(e) as being anticipated by Vachula et al (U.S. 6,458,585) is withdrawn in light of applicants arguments. Applicant traverses the rejection of claims 23, 24, 27, 28, 29, 30, 32, 37, 40, 41, 43 and 44 are rejected under 35 U.S.C. 102(e) as being anticipated by Vachula et al (U.S. 6,458,585). Applicant states that both an Exhibit A and B have been provided. Unfortunately, no exhibits can be found in the instant file. Applicant argues that the exhibits were supported by originally filed Figure 2, and states that the cells of Vachula et al are not haploidentical because they do not differ in HLA genotype as indicated in Figure 2. This has been considered and found persuasive. Accordingly the obviousness-type rejections based on Vachula et al are withdrawn.

All other rejections and objections as set forth or maintained in the prior Office action are withdrawn in light of applicants amendments and arguments.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643